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EXAMINER

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ART UNIT PAPER NUMBER

1638

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application N .

09/525,885

Applicant(s)

NUCCIO ET AL.

Examiner

Elizabeth McElwain

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03/15/00 and 09/10/01.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27³⁶ is/are pending in the application.
- 4a) Of the above claim(s) 14-39 and 44-77⁴³⁻⁷⁶ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7, 9-13 and 40-43³¹⁻⁴² is/are rejected.
- 7) ☐ Claim(s) 8 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☒ Notice of Draftperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4. 6) ☐ Other: _____

Applicant's election of Group I, claims 1-37 and 40-43 and SEQ ID NO: 2 in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

5 The requirement is still deemed proper and is therefore made FINAL.

Claims 1-13, ^{39 42}~~40-43~~ are drawn to the elected invention of Group I and SEQ ID NO:2 and have been examined on the merits.

Claims 1-13, ^{39 42}~~40-43~~ are objected to for reciting limitations drawn to non-elected inventions.

10 The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15 Claims 9-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9-13 are indefinite in the recitation of "at least about", given that it is unclear what range is covered by the term "about". Therefore, it remains unclear what the lower limit of the range would actually be.

20

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Rule 126
Claims 1-7, 9-13 and ³⁹⁻⁴²~~40-43~~ are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to isolated nucleic acid molecules that encode an enzyme having phosphoethanolamine N-methyltransferase (PEAMT) activity that comprises at least 27 contiguous amino acids of SEQ ID NO:2 or is at least 85% identical to SEQ ID NO:2. However, the specification does not set forth what structural or physical features of this sequence result in the claimed activity, and therefore the specification only provides a written description of one plant PEAMT gene from spinach that encodes a protein having the sequence of SEQ ID NO: 2, but does not adequately describe the structural features that would define any other plant PEAMT gene or amino acid sequences. In fact, the specification teaches the complexity of PEAMT, which has three different enzyme activities (pages 90-91), and that the spinach enzyme is novel, given that there was no precedent for one protein having all three of these activities. Yet, the specification does not teach which nucleotide or amino acid sequences are critical to a PEAMT, such that all three enzyme activities are exhibited.

It is well established that sequence similarity is not sufficient to determine functionality of a DNA coding sequence. See the teachings of Doerks (TIG 14, no. 6: 248-250, June 1998), where it states that computer analysis of genome sequences is flawed, and "overpredictions are common because the highest scoring database protein does not necessarily share the same or

even similar functions” (the last sentence of the first paragraph of page 248). Doerks also teaches homologs that did not have the same catalytic activity because active site residues were not conserved (page 248, the first sentence of the last paragraph). In addition, Smith et al (Nature Biotechnology 15:1222-1223, November 1997) teach that “there are numerous cases in which
5 proteins of very different functions are homologous” (page 1222, the first sentence of the last paragraph). Also, Brenner (TIG 15, 4:132-133, April 1999) discusses the problem of inferring function from homology, stating that “most homologs must have different molecular and cellular functions” (see the second full paragraph of the second column of page 132, for example). Furthermore, Borks (TIG 12, 10:425-427, October 1996) teaches numerous problems with the
10 sequence databases that can result in the misinterpretation of sequence data.

More specifically, identification of related sequences that will encode enzymes having a particular activity is particularly problematic in the enzymes involved in modifying fatty acids, and cannot be determined merely by similarity of DNA or amino acid sequences. Van de Loo et al teach that sequences encoding fatty acid hydroxylase activity are highly similar to other
15 sequences that do not encode a hydroxylase, but instead encode a fatty acyl desaturase (see the abstract, at least). In fact, Broun et al teach that a change in only four amino acids will convert a desaturase gene to a hydroxylase gene (see the abstract, at least). Thus, if sequences are identified only by similarity to other sequences that are known to encode PEAMT activity, one cannot conclude on this basis alone that these sequences also will encode a protein having said activity
20 without additional evidence of the functionality or more knowledge of the particular structural features that are required for conferring this function. Therefore, identification of genes encoding

enzymes having PEAMT activity that comprises at least 27 contiguous amino acids of SEQ ID NO:2 or are at least 85% identical to SEQ ID NO:2 are not adequately described.

See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir.

5 1997), where it states:

“The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent
10 pertaining to that cDNA’s relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA . . . Accordingly, the specification does not provide a written description of the invention . . .”

15 Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed genus, and given the high level of unpredictability of identifying genes that encode enzymes that exhibit PEAMT activity other than that exemplified in the specification, one skilled in the art would not have been in possession of the genus claimed at the time this application was filed.

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~~39-42~~
39-42

Claims 1-7, 9-13 and ~~40-43~~ 39-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for one sequence from spinach, designated PEAMT (encoding SEQ ID NO: 2), that has PEAMT activity (see pages 90-91 of the specification) does not reasonably provide enablement for any gene that encodes an enzyme that exhibits PEAMT
25 activity that comprises at least 27 contiguous amino acids of SEQ ID NO:2 or is at least 85% identical to SEQ ID NO:2. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

A showing of homology to sequences having known functional activity is not sufficient to determine the functionality of related sequences, as stated *supra*. Thus, if sequences are
5 identified only by similarity to other sequences that are known to encode PEAMT activity, one cannot conclude that these other sequences also encode enzymes having PEAMT activity, particularly having all three enzyme activities that characterize the the disclosed sequence from spinach (SEQ ID NO: 2). The specification only discloses the one sequence that encodes a
10 PEAMT, and the specification fails to provide guidance with regard to isolating and identifying other related sequences. Therefore, the identification of other genes encoding PEAMT activity is highly unpredictable.

In addition, the specification fails to teach how one would use partial sequences, including those as small as those that would encode 27 contiguous amino acids. However, the specification teaches that PEAMT has three enzymatic activities, one methyl transferase activity
15 in the N-terminal end, and two methyl transferase activities in the C-terminal end. Therefore, it is unclear how portions of a PEAMT would be used, given that it is unclear what enzyme activity, if any, would be present in any 27 contiguous amino acid fragment.

Thus, given the unpredictability of identifying sequences that exhibit PEAMT activity; the lack of guidance in the specification for identifying and characterizing any other sequences
20 that exhibit PEAMT activity; the lack of working examples, other than SEQ ID NO:2, of a sequence that encodes a protein having PEAMT activity or for the use of any fragments thereof;

given the state of the prior art, which does not teach the characteristics of a PEAMT that has three enzyme activities; and the breadth of the claims, which encompass all isolated nucleic acid molecules that encode PEAMTs that comprise at least 27 contiguous amino acids of SEQ ID NO:2 or are at least 85% identical to SEQ ID NO:2; it would require undue experimentation by one skilled in the art to make and use the invention as broadly claimed.

Claim 8 is objected to for depending on a rejected base claim, but would be in condition for allowance if written in independent form.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth F. McElwain whose telephone number is (703) 308-1794. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310. The fax phone number for this Group is (703) 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth F. McElwain, Ph.D.
November 15, 2001

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600

